

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

***APPLICATION NUMBER:***  
**20-452**

**MICROBIOLOGY REVIEW**

# **Product Quality Microbiology Review**

## **Review for HFD-150**

**26 MAR 2003**

**NDA: 20-452**

### **Drug Product Name**

**Proprietary: Paraplatin** ~~—~~

**Non-proprietary: Carboplatin solution**

**Drug Product Classification: Anti-neoplastic**

**Review Number: 2**

### **Subject of this Review**

**Submission Date: 11 OCT 2002**

**Receipt Date: 15 Oct 2002**

**Consult Date: 08 JAN 2003**

**Date Assigned for Review: 17 JAN 2003**

### **Submission History (for amendments only)**

**Date(s) of Previous Submission(s): 31 MAR 1994**

**Date(s) of Previous Micro Review(s): 4 OCT 1994**

### **Applicant/Sponsor**

**Name:** Bristol-Myers Squibb

**Address:** P.O. Box 5400  
Princeton, NJ 08543-5400

**Representative:** Noemi C. Guma, Ph.D.

**Telephone:** (609) 818-5759

**Name of Reviewer:** David Hussong

**Conclusion:** APPROVE

---

## Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUPPLEMENT:** New NDA amendment
  2. **SUPPLEMENT PROVIDES FOR:** Response to deficiencies in review dated 4 October 1994
  3. **MANUFACTURING SITE:** Bristol Caribbean, Inc.  
Mayaguez, PR 00708
  4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** 10 mg/mL solution of 10, 15 and 45 mL volumes in vials containing 50, 150 and 450 mg. The 50 mg product is in a        vial. The 150 mg product is in a        vial. The 450 mg product is in a        vial.
  5. **METHOD(S) OF STERILIZATION:**
  6. **PHARMACOLOGICAL CATEGORY:** Anti-neoplastic, cytotoxic
- B. **SUPPORTING/RELATED DOCUMENTS:** DMF        (date of update is 3 June 1997).
- C. **REMARKS:** This amendment responds to review comments from 1994. The original NDA described the aqueous form of a lyophilized product (NDA 19-880). The review of the original NDA noted that these were minor deficiencies and could be addressed as Phase 4 commitments.  
The questions shown in the amendment are different from the questions sent in the review. It is not clear where they were altered.

filename: 20-452Rv2.doc

---

**Executive Summary****I. Recommendations**

- A. Recommendation on Approvability - APPROVE**
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – N/A**

**II. Summary of Microbiology Assessments**

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – N/A**
- B. Brief Description of Microbiology Deficiencies – N/A**
- C. Assessment of Risk Due to Microbiology Deficiencies – N/A**

**III. Administrative**

- A. Reviewer's Signature \_\_\_\_\_**
- B. Endorsement Block**
  - David Hussong/Microbiologist
  - Peter Cooney/Microbiology Supervisor
- C. CC Block**
  - cc:
  - Original NDA 20-452
  - HFD- 150/Division File/NDA 20-452

3 Page(s) Withheld

**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**

---

/s/

-----  
David Hussong  
3/27/03 10:13:09 AM  
MICROBIOLOGIST

Peter Cooney  
3/27/03 11:08:35 AM  
MICROBIOLOGIST

# CONSULTATIVE REVIEW TO HFD-150

OCT 5 1994

## DIVISION OF MEDICAL IMAGING, SURGICAL, and DENTAL DRUG PRODUCTS; HFD-160

Microbiologist's Review #1

4 October 1994

A. 1. NDA 20-452

### APPLICANT

Bristol-Myers Squibb Co.  
Pharmaceutical Research Institute  
5 Research Parkway  
P.O. Box 5100  
Wallingford, CT 06492-7660

2. PRODUCT NAMES: Paraplatin® — Carboplatin —

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: A 10 mg/mL solution of 10, 15 and 45 cc volumes in vial presentations containing 50, 150 and 450 mg (respectively) for dilution into a parenteral fluid and intravenous infusion over a 6 to 8 hour period. Dose rates are based on patient surface area.

4. METHOD(S) OF STERILIZATION: \_\_\_\_\_

5. PHARMACOLOGICAL CATEGORY: Anti-neoplastic

6. DRUG PRIORITY CLASSIFICATION: 3P

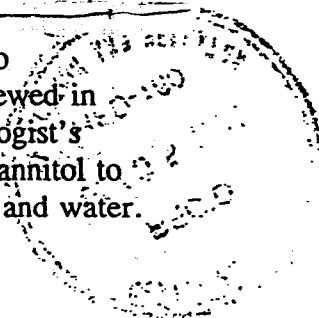
B. 1. DATE OF INITIAL SUBMISSION: 31 March 1994

2. DATE OF AMENDMENTS: 31 March 1994 and 7 April 1994

3. RELATED DOCUMENTS: NDA 19-880, Paraplatin for Injection (lyophilized) and its Microbiologist's Reviews dates 27 February 1988 and 27 January 1989.

C. REMARKS: The product represents an aqueous presentation of the same drug for a lyophilized dosage form (NDA 19-880, approved 3 March 89). The original submission for NDA 19-880 \_\_\_\_\_

\_\_\_\_\_ Also  
manufactured on these filling lines is Taxol (NDA 20-262) which was reviewed in December 1992 (Microbiologist's Review #1) and August 1993 (Microbiologist's Review #2). The lyophilized product contains equal quantities (w/w) of mannitol to drug substance, whereas the aqueous product contains only drug substance and water.



---

The 2 volumes of Amendment 1 contain a summary and 6 Attachments. These address \_\_\_\_\_ of stoppers and vials, \_\_\_\_\_ of filling equipment, and media fills.

- D. CONCLUSIONS: The submission is not recommended for approval. However, issues described in the Microbiologist's Letter to the Applicant may be addressed post-approval, pending a commitment by the applicant. For additional details, refer to section "E. Review Notes".

151  
\_\_\_\_\_  
David Hussong, Ph.D.

cc:

Original NDA 20-452  
HFD 160/Consult File  
HFD 150/Division File  
HFD 150/CSO/D.Daproza  
HFD 150/Chemist/E.Tolgyesi  
drafted by: D.Hussong, 10/04/94  
R/D initialed by: P.Cooney, 10/05/94

151



9 Page(s) Withheld

,